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On page 18, amend the paragraph bridging lines 11-20 to read as follows:

Oligodeoxyribonucleotide sequences directed toward the translation initiation site of human c-raf-1 cDNA were synthesized at Lofstrand Labs Limited (Gaithersburg, MD, USA) using beta-cyanoethyl phosphoramide chemistry on a Biosearch 8450 DNA synthesizer. The sense (ATG-S) and antisense (ATG-AS) raf ODN sequences were g'-GCAT-CAATGGAGCAC-3' (SEQ ID NO:3) and 5'-GTG-CTCCATTGATGC-3' (SEQ ID NO:4), respectively. One terminal base linkage at each end was modified to a phosphoramide group using 3H-1, 2-benzo-dithiole-3-1, 1,1-dioxide as the sulferizing agent. Oligos were synthesized at the 15 µm scale and purified on reverse phase chromatography columns,. For quality control, a small aliquot of each oligo preparation was <sup>32</sup>P-end-labeled and visualized by polyacrylamide gel electrophoresis (20% acrylamide and 5% bis) followed by densitometric scanning of the labeled products.

On page 30, amend the paragraph bridging lines 22-28 to read as follows:

A 20-mer phosphorothioate antisense ODN (ISIS 5132/5132: 5'-TCC-CGC-CTG-TGA-CAT-GCA-TT-3' (SEQ ID NO:4) corresponding to the 3' untranslated region (3'-UTR) of human c-raf-1 mRNA and a seven base mismatched phosphorothioate antisense ODN (SS 10353/10353; 5'-TCC-CGC-GCA-CTT-GAT-GCA-TT-3' (SEQ ID NO:5) were designed and synthesized as described previously (Monia et al., 1996a,b). A 20-mer phosphorothioate sense ODN (5'-ATT-GCA-TGT-CAC-AGG-CGG-GA-3' (SEQ ID NO:6)) was synthesized at Loftstrand Labs Limited (Gaithersburg, MD) as described previously (Soldatenkov et al., 1997)

## Remarks

The application is amended to comply with the requirements of 37 CFR §§ 1.821-1.825. To this end, a sequence listing is submitted herewith and the application is amended to direct its entry into the application. The specification also is amended to correct typographical errors.

The sequence listing is in the form of both a paper copy and a computer readable copy on a computer diskette. The undersigned hereby verifies that the content of the paper copy and the computer readable copy, as concurrently being submitted, are the same. The sequence listing lists sequences disclosed in the specification on pages 5, 18, and 30.

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Accordingly, amending the application to include the sequence listing adds no new matter to the application.

Also enclosed herewith is a Revocation of Former Powers of Attorney and New Power of Attorney, signed by the assignees of this application and copies of the assignments conferring rights in the signatories of the Powers of Attorney.

Lastly, the undersigned petitions in accordance with 37 C.F.R. § 1.136(a) for a three-month extension of time, inclusive of February 6, 2003, to respond to the Notice (which set an extendible period for response through October 6, 2002). While additional time is not believed to be necessary, should the Commissioner deem that an additional extension of time is needed, the undersigned hereby petitions for an additional extension of time necessary to render this submission timely.

The Commissioner is hereby authorize to charge the amount of \$ 465.00 for a three-month extension of time, as well as any additional amount that may be deemed due in connection with this submission, to deposit account no. 12-1216. A duplicate copy of this Submission is enclosed herewith for that purpose.

Respectfully submitted,

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Date: January 24, 2003

M: |Clients|Georgetown|Seq|219604 Seq listing